REMARKS

The August 12, 2002 Official Action (Paper No. 22) has been carefully considered. In view of the amendment presented herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that a shortened statutory response period of three (3) months was set in the August 12, 2002 Official Action. The initial due date for response, therefore, was November 12, 2002. A petition for a one (1) month extension of the response period is submitted with this response, which is being filed within the first month extension period.

In the August 12, 2002 Official Action, the rejections of claims 37-50 of 35 U.S.C. §112, first paragraph based on alleged lack of written description and inadequate enablement have been maintained and made final, and the rejection of claims 41 and 46-48 under 35 U.S.C. §102(a) as allegedly anticipated by U.S. Patent No. 5,616,318 to Dudney has been withdrawn.

In accordance with the present amendment, claim 37 has been amended to characterize the pesticidal agent of this invention as a "proteinaceous material". Support for this amendment is provided in the present specification, page 2, line 25 through page 3, line 15 and at page 9, lines 18-26.

As the present claim amendment is clearly supported by applicants' original specification, this amendment does not constitute new matter.

Entry of the foregoing amendment is respectfully

requested, inasmuch as this amendment is believed to place the application in condition for allowance. In any case, the present amendment should materially reduce the issues requiring consideration on appeal, should an appeal be necessary in this case.

For the reasons set forth below, the grounds of rejection maintained in the August 12, 2002 Official Action are again respectfully traversed.

Considering first the rejection based on alleged lack of written description, as the Examiner aptly points out at the top of page 7 of the August 12, 2002 Official Action, the adequacy of the written description provided in a given specification must be determined on the merits of each case. Thus, the cited passages from cases such as University of California v. Eli Lilly & Company and Fiers v. Revel, arising out of entirely different factual contexts, are of little, if any, pertinence to the present case. It has long been held that the relevant inquiry in determining compliance with the written description requirement of 35 U.S.C. §112, first paragraph, is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that, as of the filing date of the application, applicants had possession of the claimed subject matter. In re Kaslow, 218 U.S.P.Q. 1089 (Fed. Cir. 1983). In the present case, it is clear from applicants' specification that this inquiry must be answered in the affirmative. The present specification clearly conveys to a

person of ordinary skill in the art that, as of the filing date of this application, applicants were in possession of an isolated pesticidal agent which is an extracellular proteinaceous material that was obtained from a *Xenorhabdus nematophilus* species encoded by the nucleotide sequence of Figure 2 and that has toxic activity when administered orally to an insect.

Whether or not applicants provided sequence information identifying the proteinaceous material, or established that the pesticidal activity is attributable to one or two or more proteins is inconsequential to satisfying the written description requirement. Applicants provided other information indicating their possession of the claimed invention that clearly satisfies the written description requirement. Applicants have not merely identified the organism responsible for producing the observed pesticidal activity, but also have:

A. Provided a reference sequence encoding a toxin having demonstrated oral activity (Seq ID No 1 from clone 1 of NCIMB 40887 - see Examples 7 to 9);

B. Most importantly, demonstrated that the toxicity may be transferred to other organisms by genetic engineering, through use of Seq ID No 1, and still retain the unexpected oral toxicity (see Examples 7 to 9);

C. Further demonstrated that other *Xenorhabdus* sources contain closely related sequences which are identified using hybridization (note the 11.4 kb and 9 kb fragments of NCIMB 40886 and ATCC 19061 discussed of in Example 11); and

D. Also identified effective techniques which the skilled person could use should they wish to dissect out fragments of Seq ID No 1 which retained pesticidal activity (page 8, first two paragraphs). As urged in the applicants' response to the November 20, 2001 Official Action, later authors, including some of the present inventors, used precisely the techniques disclosed at page 8 of this specification, i.e. transposon mutagenesis, as taught by Siefert et al (1986) to identify sub-regions showing particular activity, as shown in Morgan et al. (2001) Applied & Environmental Microbiology p 2062-2069.

Although the present specification does not disclose using the bacteriophage P_L promoter to detect activity of the xptA1 protein as noted by the Examiner, the specification does disclose the use of the T7 and T3 promoters to detect the activity of the xptA1 protein. Specifically at page 22, lines 7-26, Applicants disclose that the DNA fragments were cloned into the SuperCos I vector of Startagene and transformed into *E. coli*. Supernatants from these transformed *E. coli* were tested for effects on the survival of *P. brassicae* larvae, thereby indicating the present of the insecticide. The SuperCos I vector utilizes T7 and T3 promoters for transcription of the inserted DNA. T7 and T3 promoters are functional equivalents of the P_L promoter as is well known in the art. Thus, the lack of disclosure of using a P_L promoter in the present specification is of no consequence as the use of a P_L promoter for subcloning is

routine in the art.

Applicants vigorously dispute the Examiner's contention that the present specification does not disclose the killing of insects via the ingestion of a proteinaceous material *per se*, but rather through the use of cells and supernatants. At page 16, lines 18-26 of the specification, it is disclosed that various treatments effect the activity of the supernatant. The displayed properties are clearly characteristic of a proteinaceous material. Specifically, the component of the supernatant is found to be temperature sensitive with complete loss of activity at 80° C. The temperature profile is characteristic of proteins as secondary and tertiary structures, which are critical to the proteins' function, are typically distorted or lost at these temperatures. Furthermore, acetone and low levels of SDS are commonly known as protein denaturants and therefore the loss of activity in their presence is again indicative of a proteinaceous material. Conversely, Triton X-100 and nonidet P40 are known to be a mild, nonionic detergents that assist the solubilization of proteins, but are regarded as non-denaturing. The inability of these treatments to reduce the activity of the supernatant further indicates that the compound of interest is proteinaceous. Similarly, cold storage and the addition of 1M NaCl are treatments that typically do not negatively impact a protein's activity. These treatments were also determined not to effect the activity of the supernatant thereby indicating a proteinaceous compound. It would be appreciated by a skilled

artisan that the combination of the results from all of the above mentioned treatments overwhelmingly point to a proteinaceous material as the agent responsible for the pesticidal activity produced by the supernatants.

Additionally, the Applicants disagree with the Examiner's position that there is not clear evidence that the toxic protein functions via the oral route. Applicants assert that because the toxin is provided to the larvae as a part of their food source that it can be determined that the method of action is via the oral route.

Turning to the alleged insufficiency of enablement provided by the present specification, the Examiner's position in this regard is plainly not well founded, considering that applicants have provided methods of both producing an using the claimed pesticidal agent directly from the *Xenorhabdus*, as set forth in Examples 1-6 of the specification. These examples, must be considered in conjunction with the additional data provided in applicants' specification, as noted above, showing that other *Xenorhabdus nematophilus* sources contain closely related sequences which were identified using hybridization and that these organisms encode the same unexpected hybrid activity of SEQ. ID No. 1, as set forth in Examples 6-9 of the present specification. Thus, the overall disclosure of applicants' specification clearly provides enablement that is commensurate in scope with the claimed invention.

To deny applicants' patent protection to which they are clearly entitled because they have not provided specific protein sequence information or identified that the pesticidally active agent is one or two or more proteins is without adequate justification and manifestly unfair.

It will almost always be true that a given sequence (even a single gene sequence) in a patent application can be to some extent modified or truncated while still retaining some activity. However this is no justification for refusing claims based on that sequence simply because they may exclude others from using such sub-sequences. The grant of such an exclusive right is appropriate because it protects the contribution to the art of the longer sequence and its activity which will have motivated the use of any shorter sequence. This is so even if shorter sequences might themselves be patentable. This is a well established principle in patent law. Furthermore, in this connection, the Examiner should appreciate the commercial reality which is that the pesticidal agents of this invention are most likely to be practiced through genetic engineering. Protection commensurate with this contribution to the art should thus be claims encompassing genetic engineering uses of Seq ID No 1, or sequences closely related to it or otherwise derived from it e.g. by taking the ORFS easily identified within it, so that the granted patent cannot be easily avoided by such simple expedients as a single base change, a truncated sequence, or the use of hybridizing homologues. This is the invention which the

applicants made, disclosed, and which is set out in the present claims, and on which patent protection is clearly warranted.

In view of the present amendments and the foregoing remarks, all of the claims now pending in this application are believed to be allowable. Accordingly, the issuance of a Notice of Allowance is in order, and such action is earnestly solicited.

Respectfully submitted,

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Marked-Up Version of Amended Claim 1

37. (Twice Amended) An isolated pesticidal agent which is an extracellular [protein] proteinaceous material obtainable from a *Xenorhabdus nematophilus* species and which is encoded by the nucleotide sequence of Figure 2 (SEQ ID No 1) or encoded by a variant obtained from *Xenorhabdus nematophilus*, the sequence of said variant hybridizing with said sequence of Figure 2 under stringent conditions, said [protein] proteinaceous material having toxic activity when administered orally to an insect.